I. General Information

CAS Number:	104-38-1
Common Name:	Hydroquinone bis(2-hydroxyethyl)ether

II. Physicochemical Data

A. Melting Point

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Remarks:	None

Method

Method:	Calculated value
Remarks:	None

Results

Melting Point Value:	101.5-102.3°C
Remarks:	None

Reference

Pirrung, M. C. and D. S. Nunn. 1996. Tetrahedron, CODEN: TETRAB, 52 (16): 5707-5738. BABS-6023959.

Other

B. Boiling Point

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Remarks:	None

Method

Method:	Estimation
Remarks:	Adapted from Stein & Brown method

Results

Boiling Point Value:	343.86°C
Remarks:	None

Reference MPBPWIN v1.40 (EPI Suite™ v.3.10). Downloadable at http://www.epa.gov/oppt/exposure/docs/episuitedl.htm ©2000 U.S. Environmental Protection Agency.

Other

C. Vapor Pressure

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Purity:	98 %
Remarks:	None

Method

Method:	OECD TG 104
Remarks:	Three saturator columns were prepared by mixing crushed glass and HQEE in an approximate ratio of 1:2. The mixture was then added to the saturator columns, the columns were attached in series to the gas flow and thenplaced in an oven adjusted to approximately 45^{o} C, 50^{o} C, or 60^{o} C, and the flow of nitrogen was adjusted to approximately 1.0 mL/minute. The nitrogen flow through the columns was continued for 14 to 26 hours. The post column flow was scrubbed through gas wash bottles filled with 100 mL of HPLC grade water. Water from the gas wash bottles was then analyzed for HQEE. Vapor pressure was calculated according to the formula: $p = (W/V)(RT/M_r)$, where: p = vapor pressure in Pa W = mass of adsorbed test substance in g V = volume of saturated gas in m^3 R = universal molar gas constant (8.206 x 10^{-5} m^3atm/mol.K) T = temperature in K M_r = relative molecular mass (198 g/mol)

Results

Vapor Pressure	
Value:	< 0.0034 mmHg at 60^{o} C and below.
Remarks:	None

Reference

Ward, T. J., C. C. Rondon and R. L. Boeri. 2004. HQEE [Hydroquinone bis (2-hydroxyethyl) ether]: Vapor Pressure Curve (Gas Saturation Method). T. R. Wilbury Labs, Inc., Marblehead, MA. Study Number 2680-AR.

D. Partition Coefficient

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Remarks:	None

Method

Method:	Estimation
Remarks:	None

Results

K_{ow}:	0.61
Remarks:	None

Reference KOWWIN v.1.66. (EPI Suite™ v.3.10). Downloadable at http://www.epa.gov/oppt/exposure/docs/episuitedl.htm ©2000 U.S. Environmental Protection Agency.

Other

E. Water Solubility

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Remarks:	None

Method

Method:	Calculated value
Remarks:	None

Results

Value:	11,695 mg/l
Temperature:	25°C
Remarks:	None

Reference Molyneux, P. and S. Vekavakayanondha. 1986. J. Chem. Soc. Faraday Trans. 1. Vol. 82: 291-318.

Other

III. Environmental Fate Endpoints

A. Photodegradation

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Remarks:	None

Method

Method:	Estimation
Test type:	Atmospheric oxidation
Remarks:	None

Results

Hydroxyl radicals reaction:	
OH Rate Constant:	40.9385 x 10^{-12} cm^3/molecule-sec
Half-life:	0.261 days (12-hr day; 1.5 x 10^6 OH/cm^3
Temperature:	25^0C
Ozone reaction:	No ozone reaction estimation was noted.
Remarks:	None

Conclusions The material is expected to rapidly degrade in the atmosphere.

Reference AopWin v1.90. (EPI Suite™ v.3.10). Downloadable at http://www.epa.gov/oppt/exposure/docs/episuitedl.htm ©2000 U.S. Environmental Protection Agency.

Other

B. Stability in Water

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Purity:	> 99%
Remarks:	None

Methods

Method:	OECD TG-111
Type:	Hydrolysis as a function of pH
GLP:	Yes
Year:	2003
Remarks:	Hydrolysis of HQEE was determined at 3 different pH values; 4.0, 7.0 and 9.0. The pH 4 solution was prepared as a 0.01 M sodium acetate buffer. It was prepared by weighing 0.82 grams of anhydrous sodium acetate into a l liter volumetric flask and adding 900 mL of distilled water. The pH was adjusted to 4.0 with concentrated acetic acid and diluted to the mark with distilled water. pH 7.0 solution was prepared as a 0.01 M phosphate buffer. It was prepared using 1.4 grams of potassium phosphate monobasic crystal per liter of solution. The pH was adjusted to 7.0 with 1 N sodium hydroxide and/or hydrochloric acid and diluted to the mark with distilled water. pH 9.0 solution was prepared as a 0.025 M sodium borate buffer. It was prepared by weighing 9.5 grams of sodium borate decahydrate into a 1 liter volumetric flask and adding 900 mL of distilled water. The pH was adjusted to 9.0 with sodium hydroxide and/or hydrochloric acid and diluted to the mark with distilled water. The buffers were autoclaved prior to use in order to remove any microbes and oxygen from the solutions. A preliminary test was conducted to determine the saturation concentration of the test material. It was determined to be 5,120 mg/l. For the main study the concentration of HQEE was 28 mg/l, which is less than the approximate half-saturation concentration and less than 0.01 M based on a molecular weight of 198. At each pH, 500 ml of test solution was subdivided into 33 vessels each containing 14 ml. The vessels were tightly capped, wrapped in aluminum foil to

exclude light, and incubated at 50 ± 1° C in a water bath. Three vessels were taken at each time point (0, 0.5, 1.0, 1.5, 3.25, 3.75, 24, 48, 72, 96, and 120 hours) and analyzed for the test substance. Appropriate controls were used as blanks for analysis.

Results

At pH 4, 7, and 9 the average measured concentration of the test article after 5 days residence in water at 50° C was 27.6, 29.1, and 29.2 mg/l, respectively. The data for all time points is presented in table 1. Each value is the mean ± standard deviation of 3 replicates.

Table 1. Measured Concentration of HQEE (mg/l)

Time (hours)	pH 4.0	pH 7.0	pH 9.0
0	28.4±0.1	28.2±0.3	28.2±0.5
0.5	28.5±0.3	28.2±0.3	28.6±0.3
1.0	28.4±0.2	28.5±0.5	28.7±0.4
1.5	28.3±0.1	28.5±0.5	28.7±0.5
3.25	28.5±0.1	28.7±0.2	28.2±0.1
3.75	28.5±0.1	28.2±0.4	28.5±0.5
24	28.3±0.2	28.3±0.1	28.5±0.2
48	28.4±0.1	28.7±0.2	28.7±0.4
72	28.0±0.2	28.7±0.3	28.7±0.3
96	27.9±0.2	29.0±1.8	28.6 ±0.3
120	27.6±0.3	29.1±0.4	29.2±0.4

Conclusions HQEE is considered to be hydrolytically stable ($t_{1/2}$ > 1 year) based on the recovery of > 90 % of the test article from 5 day old samples in water buffered to pH 4, 7, or 9.

Data Quality

Reliability: 1A

Remarks: Reliable without restrictions; Guideline study (OECD TG-111).

References

Ward, T. J., C. C. Rondon, and R. L. Boeri. 2003. HQEE [Hydroquinone bis(2-Hydroxyethyl)Ether], CAS # 104-38-1: Hydrolysis as a Function of pH. T. R. Wilbury Laboratories, Inc. Study Number 2565-AR. Marblehead, MA.

Other

C. Biodegradation – Entry 1 of 2

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Purity:	98 %
Remarks:	None

Method

Method:	OECD TG-301B
Test type:	Determination of ready biodegradability using the modified Sturm test.
GLP:	Yes
Year:	2004
Contact time:	28 days
Inoculum:	Microorganisms obtained from fresh activated sludge obtained from the municipal waste treatment facility at Newburyport, MA.
Remarks:	Six test vessels (2.5 L amber glass bottles) were used for the test – 2 for inoculated basal salts medium (BSM) (blank), 1 for the positive control (sodium benzoate), 1 for the toxicity control and 2 for the inoculated replicate test solution. Each test vessel was filled with 1,235 mL of BSM and 15 mL of activated sludge supernatant inoculum. This mixture was aerated for approximately 24 hours to purge the system of carbon dioxide. The test substance was tested at 10 mg/L total carbon. The pH of the solution was 7.5. After mixing, the solution was added to the test vessel. The final volume in each test vessel was 1,500 mL. The test was performed at a target temperature range of 22 ± 2^{o} C. The CO_2 produced was captured using absorber bottles containing $Ba(OH)_2$ connected in series to the exit air line of each vessel.

Results

Degradation %:	The positive control yielded 93 % of the theoretical CO_2, demonstrating the adequacy of the inoculum and the toxicity control allowed 43 % biodegradation after 14 days and 48 % after 28 days, indicating that HQEE was not inhibitory to the activated sludge at the tested concentration. Following a 28-day exposure to the activated sludge, only 9 % of the HQEE was biodegraded.

These results indicate that HQEE is not readily biodegradable under these test conditions.

	Degradation Rate (%)	
Sample time (day)	Test Article	Positive Control
2	5.8	39.2
5	6.2	71.0
7	7.8	80.2
9	7.7	84.6
12	7.5	87.8
16	7.7	89.8
19	8.1	91.4
23	7.2	92.2
26	8.0	92.0
27	8.4	92.2
28	9.0	92.8

Classification: The test article is not readily biodegradable under the definition of this test.
Kinetic: Not stated
Breakdown products: Not stated
Remarks: The positive control had a dissolved organ carbon removal exceeding 90% within 28 days. This fulfills the requirements of a valid test.

Conclusions The results indicate that the test material is not readily biodegradable under the conditions of this test.

Data Quality

Reliability: 1A
Remarks: Reliable without restrictions; Guideline study (OECD TG-301B).

Reference

Boeri, R. L. and T. J. Ward. 2004. Hydroquinone bis(2-hydroxyethyl)ether: Determination of the Ready Biodegradability (Biotic Degradation) Using the CO_2 Evolution Test (Modified Sturm). T.R. Wilbury Laboratories, Inc., Marblehead, MA. Report # 2682-AR.

Biodegradation – Entry 2 of 2

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Purity:	> 99.9%
Remarks:	None

Method

Method:	OECD TG-302B
Test type:	Zahn-Wellens/EMPA test for inherent biodegradability.
GLP:	Yes
Year:	1995
Contact time:	28 days
Inoculum:	Microorganisms obtained from mixed liquor suspended solids from Van Lare Waste Water Treatment Plant, Rochester, NY.
Remarks:	The test article solution (500 ml) was prepared in duplicate using 2-L Erlenmeyer flasks. The positive control solution (sodium benzoate) was prepared using a single Erlenmeyer flask. The theoretical concentration of test article and positive control was 50 mg DOC/L. Another flask served as a blank control. The vehicle was mineral nutrient solution. The incubation temperature was 21-22^0 C. All vessels were inoculated with 100 ml of the inoculum to achieve 0.2 – 1.0 g/L of suspended solids in the final test solution. The DOC, pH and dissolved oxygen were determined on days 1, 4, 6, 8, 11, 15, 18, 22, 25, 27 and 28. DOC concentrations were determined in triplicate using a Dohrmann DC-180 Carbon Analyzer. The instrument was calibrated using a 10 ppm organic carbon standard. The DOC concentrations were determined to nearest 0.1 mg/L and expressed as the arithmetic mean.

Results

Degradation %:	The starting DOC concentration of the test article solutions A and B and the positive control was 40.8 ppm, 42.6 ppm and 41.2 ppm, respectively. On day 28, DOC concentration for test article solutions A and B and the positive control was 1.0 ppm, 1.3 ppm and 3.4 ppm, respectively. These values

represent a loss of 97 % DOC for the test article and 92 % DOC for the positive control.

	Degradation Rate (%)	
Sample time (day)	Test Article	Positive Control
1	16	96
4	1	87
6	3	68
8	0	105
11	11	102
15	65	99
18	97	99
22	95	96
25	101	87
27	101	99
28	97	92

Classification: The test article is inherently biodegradable under the definition of this test.

Kinetic: Not stated

Breakdown products: Not stated

Remarks: The positive control had a DOC removal exceeding 70% within 14 days. This fulfills the requirements of a valid test. No protocol deviations were noted.

Conclusions

The results indicate that the test material undergoes rapid biodegradation and would not be expected to be persistent in the environment.

Data Quality

Reliability: 1A

Remarks: Reliable without restrictions; Guideline study (OECD TG-302B).

Reference

Lawrence, D. L. and C. J. Ruffing. 1995. Determination of Inherent Biodegradability (Biotic Degradation) Using the Zahn-Wellens/EMPA Test. Environmental Sciences Section, Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY. Study No. EN-111-023646-1.

Other

D. Transport between Environmental Compartments (Fugacity)

Test Substance

Identity: Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)

Remarks: None

Method

Method: Estimation
Model: Level III Fugacity Model
Remarks: None

Results

Estimated distribution and media concentration:		Mass Amount (%)	Half-Life (hr)	Emissions (kg/hr)
	Air	0.000415	6.27	1000
	Water	43.7	360	1000
	Soil	56.2	360	1000
	Sediment	0.0754	1.44×10^3	0

Remarks: Input values:

- Molecular weight – 198.22
- Vapor pressure – 0.0034 mmHg
- Melting point – 102°C
- Henry's LC – 1.29e-011 atm-m^3/mole
- Boiling point – 343°C
- Water solubility – 11,690 mg/l
- Log K_{ow} – 0.61
- Soil K_{oc} – 1.67

Reference Level III Fugacity Model. (EPI Suite™ v.3.10). Downloadable at http://www.epa.gov/oppt/exposure/docs/episuitedl .htm ©2000 U.S. Environmental Protection Agency.

Other

IV. Ecotoxicity

A. Acute Toxicity to Fish

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Purity:	>99.9% initial and 99.9% final, using gas chromatography with flame ionization detection
Remarks:	None

Method

Method:	OECD TG-203
Test type:	Acute static
GLP:	Yes
Year:	1995
Species/strain:	Fathead minnow (*Pimephales promelas*)
Analytical monitoring:	The concentration of the test substance was determined analytically using high performance liquid chromatography with an ultraviolet detector. The test substance was measured at study time 0 and 96 hours.
Exposure period:	96 hours
Statistical methods:	The LC_{50} and 95 % confidence level at various time points (24, 48, 72, and 96 hours) during the study were determined using the following three approaches: non-linear interpolation, moving average method and probit method.
Remarks:	The test organisms were exposed to 5 analytically determined concentrations that ranged from 86 to 1044.2 mg test article/l of water. The aquatic test was performed in seamless Pyrex glass 30.5 cm cuboidal chromatography jars, each containing 20 L of exposure solution. The light/dark cycle of the photoperiod was 16 hours on/8 hours off with a 20 minute transition period. The temperature in all test vessels remained at 20 ± 1^{o} C during the test. The pH and oxygen ranged from 8.0 to 8.6 and 8.6 to 9.2 mg/l, respectively. Observations for mortality and signs of stress were made during the study at 0, 2.5, 24, 48, 72 and 96 hours. After the measurements for physical parameters were performed at time 0, the minnows were placed into each of the replicate test article concentration vessels and replicate control vessels. They were

approximately 37 days old at the start of testing. Two replicates were used for each concentration with 10 minnows per vessel for a total of 20 fish per concentration. All organisms for this test were acclimated to the diluent water prior to the test since the same filtered-treated-tempered water and filtered, compressed air used for all laboratory water/aeration processes during the test were supplied continuously to the stainless steel rearing tanks. All organisms used in this test were maintained in this water for at least two weeks before being exposed to the test article.

Results

Analytical concentrations: Mean of values determined at 0 and 96 hours of test
Control – no test article detected
86 mg/l, 168.3 mg/l, 312.8 mg/l, 570.4 mg/l and 1044.2 mg/l.

Mortality:

Percent Mortality

Concentration (mg/l)	Time (hours)				
	2.5	24	48	72	96
Control	0	0	0	0	0
86	0	0	0	0	0
168.3	0	0	0	0	0
312.8	0	5	5	5	5
570.4	0	0	0	0	0
1044.2	0	0	0	0	0

Values: LC_{50} (95% confidence limits) (mg/l)

24-hr	48-hr	72-hr	96-hr
>1043.7	>1043.7	>1043.7	>1043.7

NOEC (mg/l)

24-hr	48-hr	72-hr	96-hr
>1043.7	>1043.7	>1043.7	>1043.7

Remarks: None

Data Quality

Reliability: 1A
Remarks: Reliable without restrictions; Guideline study (OECD 203).

Reference	Lawrence, D. L. and M. P. Hirsch. An Acute Aquatic Effects Test with the Fathead Minnow, *Pimephales promelas* using Hydroquinone bis (2-Hydroxyethyl) Ether. Eastman Kodak Company, Rochester, NY. Study No. EN-430-023646-1; HAEL No. 94-0220. 1995.
Other	

B. Acute Toxicity to Invertebrates

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Purity:	>99.9% initial and 99.9% final, using gas chromatography with a flame ionization detector

Method

Method:	OECD TG-202
Type:	Acute static
GLP:	Yes
Year:	1995
Species/strain:	Water flea (*Daphnia magna*)
Analytical monitoring:	The concentration of the test substance was determined analytically using high performance liquid chromatography with ultra violet detection. The test substance was measured at study time 0 and 48 hours.
Exposure period:	48 hours
Statistical methods:	The LC_{50} and 95 % confidence level at various time points (24 and 48 hours) during the study were determined using the following three approaches: non-linear interpolation, moving average method and probit method.
Remarks	The test organisms were exposed to 5 analytically determined concentrations that ranged from 100.2 to 992.9 mg test article/l of water. The aquatic test was performed in 250-ml Pyrex glass beakers. The light/dark cycle of the photoperiod was 16 hours on/8 hours off with a 20 minute transition period. The temperature in all test vessels remained at 21^{o} C during the test. The pH and oxygen ranged from 8.1 to 8.3 and 8.4 to 8.9 mg/l, respectively. Observations signs of immobility and stress were made during the study at 0, 6, 24 and 48 hours. After the measurements for physical parameters were performed at time 0, neonate daphnids were placed into each of the replicate test article concentration vessels and replicate control vessels. Two replicates were used for each concentration with 10 daphnids per vessel for a total of 20 organisms per concentration. All daphnids for this test were acclimated to the diluent water prior to the test since the same filtered-treated-tempered water

and filtered, compressed air used for all laboratory water/aeration processes during the test were supplied continuously to the stainless steel rearing tanks. All organisms used in this test were maintained in this water for at least two weeks before being exposed to the test article.

Results

Analytical concentrations: Mean of values determined at 0 and 48 hours of test
Control – no test article detected
100.2 mg/l, 188.1 mg/l, 325.5 mg/l, 553.5 mg/l and 992.9 mg/l

Immobility:

Concentration (mg/l)	Percent Immobile Time (hours)			
	0	6	24	48
Control	0	0	0	0
100.2	0	0	5	15
188.1	0	0	0	40
325.5	0	0	0	0
553.5	0	0	0	20
992.9	0	0	0	25

Values:

EC_{50} (95% confidence limits) (mg/l)

24-hr	48-hr
>992.9	>100.2

NOEC (mg/l)

24-hr	48-hr
992.9	100.2

Data Quality

Reliability (Klimisch): 1A

Remarks: Reliable without restrictions; Guideline study (OECD TG-202).

Reference

Lawrence, D. L. and M. P. Hirsch. An Acute Aquatic Effects Test with the Daphnid, *Daphnia magna* using Hydroquinone bis (2-Hydroxyethyl) Ether. Eastman Kodak Company, Rochester, NY. Study No. EN-431-023646-1; HAEL No. 94-0220. 1995.

Other

Acute Toxicity to Aquatic Plants (Algae)

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Purity:	98 %
Remarks:	None

Method

Method:	OECD TG 201
Test type:	Acute static
GLP:	Yes
Year:	2004
Species/Strain	*Selenastreum capricornutum*/UTEX 1648
Supplier:	Culture collection of algae from University of Texas
Analytical monitoring:	Yes
Exposure period:	72 hours
Statistical methods:	Weighted least squares non-linear regression and one-way analysis of variance.
Remarks:	Algae were distributed among six replicates of the control and 3 replicates of each test concentration. Nominal concentrations of HQEE were 65, 130, 250, 500, and 1000 mg/L. Analytically measured mean concentrations were 63, 130, 250, 500, and 970 mg/L. Flasks were inoculated with approximately 10,000 cells/mL and capped with inverted glass beakers. A 24-hour light and 0-hour dark photoperiod was automatically maintained with cool-white fluorescent lights that provided a light intensity of approximately 380 to 390 footcandles. The number of cells/mL in each test vessel and the occurrence of relative size differences, unusual cell shapes, colors, flocculations, adherence of cells to test containers, or aggregation of cells was determined visually by means of direct microscopic examination at 24, 48 and 72 hours. Temperature of the incubator (24 ± 2^{o} C) was measured and recorded daily. The pH (7.5 ± 0.1) of test solutions was measured and recorded in each test solution prior to distribution to the test vessels at the start of the test and in each test vessel at the end of the test.

Results

EC_{50} (72-hour):	Average specific growth rate – >970 mg/L Number of cells/mL – 820 mg/L
Remarks:	The 72-hour NOEC is 250 mg/L when determined using the number of cells/mL and 500 mg/L when calculated using the average specific growth rate. The cells grew well at all concentrations except for 970 mg/L. At the top concentration, HQEE was algistatic rather than algicidal.

Conclusions HQEE exhibits low acute toxicity to algae.

Data Quality

Reliability:	1A
Remarks:	Reliable without restriction; OECD guideline study

Reference Boeri, R. L. and T. J. Ward. 2004. Hydroquinone bis(2-hydroxyethyl)ether: Growth and Reproduction Toxicity Test with the Freshwater Alga, *Selenastrum capricornutum*. T.R. Wilbury Laboratories, Inc., Marblehead, MA. Report # 2681-AR.

Other

V. Mammalian Toxicity

A. Acute Toxicity – Entry 1 of 2

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Purity:	Not stated
Remarks:	None

Method

Method/guideline followed:	Not stated
Type:	Oral toxicity
GLP:	Yes
Year:	1989
Species/Strain:	Rat/Crl:CD (SD)BR
Sex:	Male/Female
Number of animals/ sex/dose:	5
Vehicle:	0.5% aqueous guar gum
Route of administration:	Oral (gavage)
Remarks:	One group of 10 rats (5M, 5F) was administered the test substance (25 % concentration in vehicle) at a dose of 5 g/kg. Animal weight was 182-197 g for males and 164-173 g for females. Animals were observed for mortality and clinical signs for 15 days.

Results

Value:	LD_{50} is greater than 5 g/kg
Mortality rate:	No mortality
Remarks:	All animals appeared normal with no incidence of clinical signs of toxicity. All animals gained weight normally. No treatment-related changes were noted at necropsy from gross pathological examination.

Conclusions

Remarks:	The acute oral LD_{50} is greater than 5 g/kg.

Data Quality

Reliability:	2D
Remarks:	The study is reliable with restrictions. Data appear solid, but report lacks details consistent with a guideline study.

Reference

Shepard, K. P. 1989. Acute toxicity of HQEE. Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY. HAEL No. 89-0126.

Other

Acute Toxicity – Entry 2 of 2

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Purity:	Not stated
Remarks:	None

Method

Method/guideline followed:	Not stated
Type:	Dermal toxicity
GLP:	Yes
Year:	1989
Species/Strain:	Rat/Crl:CD (SD)BR
Sex:	Male/Female
Number of animals/ Sex/dose:	5
Vehicle:	Water. Test article was moistened with the vehicle.
Route of administration:	Dermal
Remarks:	One group of 10 rats (5M,5F) was administered the test substance (solid material moistened with water) at a dose of 2 g/kg. The test article was applied to the skin following hair removal with an electric clipper. An occlusive wrap was used to hold the test material against the skin for 24 hours. At the end of exposure, residual test material was washed off with water. Animal weight was 187-197 g for males and 169-191 g for females. Animals were observed for mortality and clinical signs for 14 days.

Results

Value:	LD_{50} is greater than 2 g/kg.
Mortality rate:	No mortality
Remarks:	All animals appeared normal with no incidence of clinical signs of toxicity. All animals gained weight normally. No treatment-related changes were noted at necropsy from gross pathological examination.

Conclusions

Remarks:	The acute dermal LD_{50} is greater than 2 g/kg.

Data Quality

Reliability (Klimisch):	2D
Remarks:	The study is reliable with restrictions. Data appear solid, but report lacks details consistent with a guideline study.

Reference Shepard, K. P. 1989. Acute toxicity of HQEE. Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY. HAEL No. 89-0126.

Other

B. Genetic Toxicity *In Vitro*

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Purity:	98%
Remarks:	None

Method

Method:	OECD TG 471 – Bacterial Point Mutation Assay using *Salmonella typhimurium* and *Escherichia coli*
Type:	Reverse mutation assay
Test system:	Bacteria
GLP:	Yes
Year:	2004
Species/Strain:	*Salmonella typhimurium*/TA1535, TA1537, TA100 and TA98 and *Escherichia coli* WP2uvrA
Metabolic activation:	9000 g (S9) liver homogenate from Arochlor 1254-induced male F-344 rats.
Concentrations tested:	17, 50, 167, 500, 1667, and 5000 µg/plate with and without S9 Vehicle control – DMSO Positive controls – 2-aminoanthracene, N-ethyl-N-nitro-N-nitrosoguanidine, sodium azide, 2-nitrofluorene, and 9-aminoacridine.
Remarks:	The test procedures are based on the method by Ames et al. (1975) (in reference list of cited study). Two independent tests were conducted on agar plates in the presence and absence of S-9 fraction. Concurrent positive controls demonstrated the sensitivity of the assay and the metabolizing capability of the S9 mix. Samples of each strain were grown by culturing for 16 hours at 37^{o} C in nutrient broth. These cultures were kept for up to 4 days at 4^{o} C to allow relevant checks to be performed but fresh cultures were used for the experiments. In the course of testing, 2 methods of treatment were performed to extend the range of conditions within the assay. The tests performed were the Direct Plate method and the Pre-incubation method. In the Direct Plate method volumes of soft agar were dispensed into small sterile tubes. The solvent or test solution was added last. The tube contents were mixed andpoured onto minimal

medium plates. When the soft agar had set, the plates were inverted and incubated at 37° C for 2 or 3 days. In the Pre-incubation method volumes of S9 mix or 0.05 M phosphate buffer, pH 7.4 were dispensed into small sterile tubes. This was followed by 0.1 ml of bacteria per tube and the solvent or test solution. The tube tops were then screwed on tightly and the tubes placed in a shaking incubator at 37° C for 20 minutes. The tube tops were removed and 2 ml of soft agar added to each tube. The tube contents were mixed and then poured onto agar plates, as above. After incubation, the colonies were counted and data captured electronically using a validated software system. The plates were also examined for precipitates and microscopically for microcolony growth.

Results

Result:	HQEE is not mutagenic to *Salmonella typhimurium*/TA1535, TA1537, TA100 and TA98 and *Escherichia coli*.
Cytotoxic Concentration:	None. No toxicity was observed at any concentration.
Genotoxic effects:	Negative with and without metabolic activation.
Remarks:	None

Conclusions

Remarks:	HQEE is not mutagenic to bacteria in this assay.

Data Quality

Reliability:	1A
Remarks:	Reliable without restriction; guideline study (OECD TG 471).

Reference

Blackstock, C. 2004. Hydroquinone bis (2-hydroxyethyl) Ether: Testing for Mutagenic Activity with *Salmonella typhimurium*/TA1535, TA1537, TA100 and TA98 and *Escherichia coli* WPuvrA. Inveresk Research, Tranent, Scotland. Report Number 23825.

Other

Genetic Toxicity *In Vivo*

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Purity:	98 %
Remarks:	None

Method

Method/guideline followed:	OECD TG-474
Test type:	*In vivo* Mouse Micronucleus Test
GLP:	Yes
Species:	Mouse
Strain:	CD-1
Number and sex:	5 males and 5 females in vehicle control (0.5 % carboxymethylcellulose) group; 10 males and 10 females in treatment group; 5 males in the positive control (cyclophosphamide) group. Weight range at the start of the study for males and females was 26-35 g and 21-26 g, respectively. Age ranged from 6-7 weeks.
Route of administration:	Oral gavage
Duration of test:	2 days
Dose level:	2000 mg/kg. A dose range finding study was conducted using dose levels of 50, 125, 350, 800, or 2000 mg/kg. No adverse reactions or animal deaths occurred at any dose level. 2000 mg/kg is the highest dose routinely used in this assay. Thus, this test was conducted as a limit test.
Exposure period:	24 hours – mice were dosed at 0 hour and 24 hours with bone marrow samples taken 24 hours after the second dose.
Remarks:	The test article was dissolved in the vehicle and dosed at a volume of 10 mL/kg body weight. The positive control was administered at a dose of 50 mg/kg. The animals were weighed immediately before each dose. Food was available *ad libitum* except 2-4 hour period prior to dosing and 1-2 hours post-dose. Water was available *ad libitum*. Following animal sacrifice 1 femur from each mouse was dissected and freed of adherent tissue. A small hole was made in the neck of each femur and the marrow flushed into a centrifuge tube containing an appropriate buffer solution. Routine

tissue culture antibiotics were included to prevent microbial growth. Tubes were centrifuged and all but a few drops of fluid discarded. The cells were then resuspended. A drop of the bone marrow suspension was placed at one end of the slide and a smear made. Two slides were prepared from each animal. A minimum of 2000 polychromatic erythrocytes (PCE) per animal were scored for micronuclei and the frequency of micronucleated cells (MN-PCE) determined. As a control against inclusion of artifacts, or action of a mutagen on the G_2 and/or mitotic phase of the cell cycle, the numbers of micronucleated normochromatic erythrocytes (MN-NCE) in mature red blood corpuscles were also recorded. The PCE/NCE ratio, a measure of any induced systemic toxicity, was determined by counting a minimum total of 1000 erythrocytes (PCE+NCE) per marrow preparation.

Results

Remarks: The numbers of micronucleated bone marrow polychromatic erythrocytes (MN-PCE) in mice dosed with the vehicle averaged 0.04 %. This MN-PCE frequency conformed to the established in-house control range. Exposure of mice to the positive control agent induced large increases in bone marrow micronuclei. The mean MN-PCE frequency for this group was 1.32 %. The highest MN-PCE frequency recorded for the test article was 0.05 %. There was no indication of bone marrow toxicity due to the test article based on a PCE/NCE ratio similar to the vehicle control (0.84 ± 0.09 – test article; 0.83 ± 0.17 – control).

Conclusions

Remarks: HQEE does not induce micronuclei in bone marrow cells. Thus, according to the results of this assay, HQEE does not induce chromosome aberrations

Data Quality

Reliability: 1A

Remarks: Reliable without restriction; OECD guideline study (TG-474)

Reference

Innes, D. C. 2004. Hydroquinone bis (2-hydroxyethyl) Ether: Micronucleus Test in bone marrow of CD-1 Mice 0 h and 24 h Oral Dosing and 48 h Sampling. Inveresk Research, Tranent, Scotland. Report Number 24050.

Other

C. Repeated Dose Toxicity

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Purity:	97.2% -- determined by gas chromatography with flame ionization detector
Remarks:	Stability of the test article in the diets was determined by repeated analysis on 0, 4, and 8 days and 2, 3, 4, and 5 weeks after diet preparation. Concentrations of the test article were (mean ± SD) 0.1 ± 0.02 % and 0.96 ± 0.03 % after 36 days of storage indicating the material was stable for the duration of the study. Target concentrations were 0.1 % and 1.0 %. Mean (± SD) concentrations of the diets used during the study were 0.099 ± 0.0008, 0.32 ± 0.02, and 0.98 ± 0.03 %.

Method

Method/guideline followed:	OECD TG-407
Test type:	Oral
GLP:	Yes
Species:	Rat
Strain:	CD(SD)BR
Number and sex:	5 males and 5 females/group. Weight (mean ± SD) at the start of the study for males and females was 162 ± 6 g and 146 ± 6 g, respectively.
Route of administration:	Oral (incorporation into the diet)
Duration of test:	28 days
Concentration level:	0.1, 0.3 or 1.0% (rounded) in the feed. The concentrations correspond to dose levels of 85, 249 or 848 mg/kg/day in the males and 81, 262 or 851 mg/kg/day in the females, respectively.
Exposure period:	28 days
Frequency of treatment:	Test article was continuously available throughout the 28 day exposure period.
Control group and treatment:	Yes; concurrent using diets containing 1% corn oil.
Post-exposure observation period:	None
Methods:	Body weights were collected on days 0, 3, 7, 14, 21 and 28. Feed consumption was determined on days 3, 7, 10, 14, 17, 21, 24 and 28. Clinical

observations were performed daily and included, but were not limited to, examination of fur, skin, eyes, motor activity, feces and urine. Blood was collected at necropsy for hematology (hemoglobin concentration, hematocrit, red and white blood cell count, differential white blood cell count, platelet count, red blood cell indices (MCV, MCH, and MCHC) and examination of blood smears for cellular morphology and clinical chemistry (aspartate aminotransferase, alanine aminotransferase, sorbitol dehydrogenase, alkaline phosphatase, creatining, urea nitrogen (BUN), and glucose) tests. Organ weights were taken for liver, kidneys, adrenal glands, testes, spleen, and thymus. The following tissues from the control and high dose groups were fixed in formalin and examined histopathologically: trachea, lungs, heart, esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, pancreas, liver, salivary glands, kidneys, urinary bladder, pituitary gland, adrenal glands, thyroid gland, parathyroid glands, thymus, spleen, mesenteric lymph nodes, bone marrow (femor), brain, testes, epididymides, male accessory sex glands, ovaries, vagina, uterus, fallopian tubes, and gross lesions. Mean values were calculated for body weight, feed consumption, organ weights, hematology and clinical chemistry. All mean data, except feed consumption, were evaluated using the following computer-generated statistical tests: Bartlett's test ($p \leq 0.01$), one-way analysis of variance ($p \leq 0.05$) and Duncan's multiple range test ($p \leq 0.05$) to indicate statistical significance. Feed consumption was not analyzed statistically because the animals were group housed.

Remarks: Protocol written and followed as per stated guideline with no deviations.

Results

NOAEL (NOEL): Male rats – 0.3 % in the diet (249 mg/kg)
Female rats – 1.0 % in the diet (851 mg/kg)

LOAEL (LOEL): Male rats – 1.0 % in the diet (848 mg/kg)
Female rats – Could not be determined as the NOAEL was the highest dose tested.

Remarks: No mortality occurred during the study. There were no treatment-related clinical signs of toxicity observed during the study. There were no statistical

body weight differences between any of the treated animals and control animals. Feed consumption was comparable for all animals in the treated groups and control group. In the mid-dose males hemoglobin concentration was slightly higher compared to the control males (P=0.05), but there was no dose response relationship as the hemoglobin concentration in the low- and high-dose males was not statistically significantly different from controls. The mean blood platelet count for the high-dose males was slightly less (p=0.02) than for the control group. Platelet counts were not statistically significantly different from controls in the mid- and low-dose males. No other abnormalities in hematology were noted in the males. No hematological abnormalities were observed in any of the female animals. The clinical chemistry findings in all treated animals were comparable to controls. Relative kidney weights in low- and mid-dose females were lower (p=0.02), but not different from controls in the high-dose females. Absolute kidney weights for all treated female animals were similar to controls. No other organ weight differences were seen in any dose group for either sex. No compound-related lesions were seen during gross or histopathological examinations.

Conclusions

Remarks: The test article appears to reduce the platelet count in males at the top dose (848 mg/kg). 249 mg/kg is the NOEL for this effect. The decrease in relative kidney weights in the low- and mid-dose females is judged to be of no toxicological significance for 3 reasons. Absolute kidney weights were not affected in any of treated female animals, relative kidney weights were not different from controls in the high-dose females, and no gross or histopathological change was noted in this organ from any treatment group.

Data Quality

Reliability (Klimisch): 1A

Remarks: Reliable with restrictions. Guideline study (OECD TG-407)

Reference: Hosefeld, R. S. and G. J. Hankinson. 1988. Four Week Oral Toxicity Study of Hydroquinone Bis (2-Hydroxyethyl) Ether in the Rat. Report number 87-0068. Toxicological Sciences Laboratory, Eastman Kodak Company, Rochester, NY 14650.

Other

D. Reproductive/Developmental Toxicity

Test Substance

Identity:	Hydroquinone bis (2-hydroxyethyl) ether (CAS RN 104-38-1)
Purity:	99.7 %

Method

Method/guideline followed:	OECD TG-421
Test type:	Oral
GLP:	Yes
Species:	Rat
Strain:	Sprague-Dawley (Crl: CD(SD) IGS BR)
Number and sex:	10 males and 10 females/group. Weight (mean ± SD) at the start of the study for males and females was 304 ± 6 g and 195 ± 2 g, respectively.
Route of administration:	Oral (gavage). Vehicle – carboxymethylcellulose.
Duration of test:	53 days
Dose level:	100, 300, or 1000 mg/kg at a constant dose volume of 10 ml/kg/day.
Exposure period:	53 days. The males were treated for at least 4 weeks, starting 2 weeks prior to mating; treatment of females commenced 2 weeks prior to mating and continued through day 4 of lactation.
Frequency of treatment:	Once daily7 days per week.
Control group and treatment:	Yes. Control group dosed with vehicle only.
Post-exposure observation period:	None
Methods:	Body weights of males were recorded once during the week prior to dosing and once daily from commencement of treatment until termination. Female weights were recorded once during the week prior to dosing and daily form commencement of dosing throughout gestation and lactation until termination. Litter and pup weight were measured. Food consumption was measured weekly. Clinical observations were conducted daily. Organ weights were measured for the testes, epididymides and liver. Organs examined histologically were the ovary, testis and epididymis. Mating performance, fertility indices, length of gestation, implantation sites, litter performance and pup survival indices

were measured. Pups were examined for externally visible abnormalities. Body weight and food consumption data were subjected to analysis of variance or the Kruskal-Wallis non-parametric analysis. Organ weight data were analyzed by analysis of variance and analysis of covariance using the terminal bodyweight as the single covariate. Histological data were analyzed by Fisher's Exact Probability test.

Results

Maternal NOEL:	1000 mg/kg
Reproduction/ Developmental Toxicity NOEL for males and females:	1000 mg/kg
Remarks:	No mortality occurred during the study. There were no clinical observations observed that indicated a treatment-related effect from the test article. Body weight gain and food consumption in both sexes were essentially similar in all groups. There were no findings to demonstrate any effect of treatment on reproductive performance or to fetal or pup development. There were no abnormalities noted among the pups between control and any dose group. There was no effect of treatment on epididymis or testes weights between control and any dose group. There were no gross or histopathological changes noted between the control and any dose group.

Conclusions

Remarks:	Fertility, fetal development and pup survival were not affected by treatment with hydroquinone bis (2-hydroxyethyl) ether at dose levels up to and including 1000 mg/kg. Also, there were no systemic effects or gross or histopathological tissue changes observed to either males or females from exposure to this material.

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restrictions. Guideline study (OECD TG-421).

Reference: Clubb, S. K. and L Jardine. 2004. Hydroquinone bis (2-hydroxyethyl) Ether – Reproduction/Developmental Toxicity Screening Test. Inveresk Research, Tranent, Scotland. Report Number 24420.

Other